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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/963,521	ZIEGLER ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-28,30-37,39-49,51-58 and 60* is/are rejected.

7)☒ Claim(s) *29,38,50 and 59* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/431099.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 19-60 are pending.

Applicant's cancellation of claims 6-14, 16-18, and addition of claims 19-60 in a communication filed on 5/18/2004 is acknowledged.

The Examiner contacted Thomas Cawley on or about 8/2/2004 to discuss possible amendments to the claims and submission of a terminal disclaimer but no agreement could be reached.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

1. Claims 24-25, 31-34, 45-46, 52-55 are objected to due to the recitation of "wherein the Corynebacterium", "wherein the Brevibacterium", "wherein the coryneform bacteria". For clarity and consistency, it is suggested that the terms be amended to recite "wherein Corynebacterium", "wherein Brevibacterium", "wherein coryneform bacteria". Appropriate correction is required.

2. Claims 26 and 47 are objected to due to the recitation of "support page 12, line 23, 24" at the end of the claims. This appears to be a typographical error. Appropriate correction is required.

3. Claims 27-30, 35-36, 48-51, 56-57 are objected to due to the recitation of "wherein said coryneform bacteria also overexpress by...". For clarity and consistency with language commonly used in the art, it is suggested that the term be amended in claims 27-28, 30 to recite "wherein the Corynebacterium glutamicum .... gene encoding ..... is also overexpressed in said coryneform bacteria by increasing the copy number of said gene", in claim 29 to recite "wherein the Corynebacterium glutamicum hom^{dr} allele encoding a feedback-resistant homoserine dehydrogenase is also overexpressed in said Corynebacterium or Brevibacterium by increasing the copy number of said allele", in claims 35-36 to recite "wherein one or more of the coryneform genes selected from the group consisting of the

Coryneform glutamicum pyc gene encoding pyruvate carboxylase, the Coryneform glutamicum hom gene encoding homoserine dehydrogenase, the Coryneform glutamicum hom^{dr} allele encoding a feedback-resistant homoserine dehydrogenase, and the Coryneform glutamicum mqo gene encoding malate:quinone oxidoreductase are overexpressed by increasing the copy number of said genes", in claims 48-49, 51 to recite "wherein the Corynebacterium glutamicum.....gene encoding ..... is also overexpressed in said coryneform bacteria by operatively linking said gene to a promoter", in claim 50 to recite "wherein the Corynebacterium glutamicum hom^{dr} allele encoding a feedback-resistant homoserine dehydrogenase is also overexpressed in said coryneform bacteria by operatively linking said allele to a promoter", and in claims 56-57 to recite "wherein one or more of the coryneform genes selected from the group consisting of the Coryneform glutamicum pyc gene encoding pyruvate carboxylase, the Coryneform glutamicum hom gene encoding homoserine dehydrogenase, the Coryneform glutamicum hom^{dr} allele encoding a feedback-resistant homoserine dehydrogenase, and the Coryneform glutamicum mqo gene encoding malate:quinone oxidoreductase are overexpressed by operatively linking said genes to a promoter". Appropriate correction is required.

4. Claim 56 is objected to due to the recitation of "liniking" in step (a). This appears to be a typographical error. Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 20-23, 39, 41-44 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 20-23 and 41-44 are indefinite in the recitation of "wherein said Corynebacterium or Brevibacterium also are overexpressed by ..." or "wherein said coryneform bacteria also overexpress by ..." for the following reasons. As known in the art, polynucleotides, and not bacteria, are expressed or overexpressed. It is suggested that the term be amended in claims 20-21, 23 to recite "wherein the Corynebacterium glutamicum .....gene encoding ..... is also overexpressed in said Corynebacterium or Brevibacterium by increasing the copy number of said gene", in claim 22 to recite "wherein the Corynebacterium glutamicum hom^{dr} allele encoding a feedback-resistant homoserine dehydrogenase is also overexpressed in said Corynebacterium or Brevibacterium by increasing the copy number of said allele", in claims 41-42, 44 to recite "wherein the Corynebacterium glutamicum .... gene encoding ..... is also overexpressed in said Corynebacterium or Brevibacterium by operatively linking said gene to a promoter", and in claim 43 to recite "wherein the Corynebacterium glutamicum hom^{dr} allele encoding a feedback-resistant homoserine dehydrogenase is also overexpressed in said Corynebacterium or Brevibacterium by operatively linking said allele to a promoter". For examination purposes, the suggested language will be used. Correction is required.

8. Claims 39 and 60 are indefinite in the recitation of "wherein said thrE gene comprises SEQ ID NO: 1 and SEQ ID NO: 3" for the following reasons. According to the specification, SEQ ID NO: 1 represents the nucleotide sequence of the thrE gene from C. glutamicum ATCC 14752 and SEQ ID NO: 3 is the nucleotide sequence of the thrE gene from C. glutamicum ATCC 13032. While the nucleotide sequence of both thrE genes is somewhat different, they both encode the same protein, i.e. SEQ ID NO: 2. Therefore, it is unclear as to how the thrE gene can comprise both sequences, i.e. SEQ ID NO: 1 and 3, at the same time. It is suggested that the claim be amended to recite "wherein said thrE gene comprises SEQ ID NO: 1 or SEQ ID NO: 3". The suggested language will be used for examination purposes. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 35 and 56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection has been previously discussed in a Non Final Action mailed on 2/24/2004.

11. Applicants argue that the new claims submitted are directed to subject matter which is fully supported. In particular, Applicants submit that independent claims 19, 26, 33-34 are directed to a process of isolating L-threonine by overexpressing the C. glutamicum thrE gene by increasing the copy number, whereas independent claims 40, 47, 56-57 are directed to a process of isolating L-threonine by overexpressing the C. glutamicum thrE gene by operatively linking the thrE gene to a promoter.

12. Applicant's arguments have been fully considered but are not deemed persuasive to avoid the rejection of new claims 35 and 56. While it is agreed that claims 19-34, 36-55, and 57-60 limit the thrE gene to that of C. glutamicum, it is noted that in claims 35 and 56, step (a), the claim reads "fermenting L-threonine producing.....bacteria in which a thrE gene encoding a threonine exporter carrier protein is overexpressed...". There is no limitation in regard to the source of the thrE gene and thus the claims encompass practicing the claimed method with any gene encoding a threonine exporter carrier protein. For the reasons already discussed in the previous Office Action, a genus of genes encoding a threonine exporter carrier protein is not adequately described. Therefore, claims 35 and 56 are rejected for the reasons of record.

13. It is noted that this rejection may be overcome by amending the claims to recite "C. glutamicum thrE gene" instead of "thrE gene".

14. Claims 35 and 56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the preparation of L-threonine comprising fermenting L-threonine producing Corynebacterium or Brevibacterium bacteria in which the C. glutamicum thrE gene encoding a threonine export carrier protein is overexpressed by (a) increasing the copy number of said gene, or (b) operatively linking said gene to a promoter, does not reasonably provide enablement for the method described above wherein any gene encoding a threonine export carrier protein is used. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection has been previously discussed in a Non Final Action mailed on 2/24/2004.

15. Applicants refer to the remarks made in regard to the written description rejection and indicate that the new claims are fully supported and enabled by the specification.

16. As indicated above, Applicant's arguments have been fully considered but are not considered persuasive to avoid the rejection of new claims 35 and 56 in view of the fact that there is no limitation in claims 35 and 56 in regard to the source of the gene encoding the threonine export carrier protein. Thus, the claims encompass practicing the claimed method with any gene encoding a threonine export carrier protein. For the reasons already discussed in the previous Office Action, the specification does not enable a genus of genes encoding a threonine export carrier protein. Therefore, claims 35 and 56 are rejected for the reasons of record.

17. It is noted that this rejection may be overcome by amending the claims to recite "C. glutamicum thrE gene" instead of "thrE gene".

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 19-21, 23-28, 30-37, 40-42, 44-49, 51-58 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 6 of U.S. Patent No. 6596516 (common inventors Petra Ziegler, Lothar Eggeling, Hermann Sahm and Georg Thierbach). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Claims 19-21, 23-25, 35, 40-42, 44-46, 56 are directed in part to a process requiring the fermentation of L-threonine producing C. glutamicum or Brevibacterium lactum wherein the C. glutamicum thrE gene is overexpressed by increasing its copy number or by operatively linking the thrE gene to a promoter, and wherein in addition to the C. glutamicum thrE gene, the C. glutamicum pyc gene, the C. glutamicum mqo gene, and/or the C. glutamicum hom gene are also overexpressed by increasing their copy number or by operatively linking said genes to a promoter. Claim 6 of U.S. Patent No.

6596516 is directed to a fermentation process for the production of L-threonine in coryneform bacteria wherein said bacteria are modified such that one or more genes selected form the group consisting of (a) the hom gene encoding homoserine dehydrogenase, (b) the gap gene encoding glyceraldehyde 3-phosphate dehydrogenase, (c) the pyc gene encoding pyruvate carboxylase, (d) the mqo gene encoding malate:quinone oxidoreductase, and (e) the thrE gene encoding threonine export carrier protein are overexpressed, and wherein the glyA gene is attenuated. The specification in U.S. Patent No. 6596516 discloses(1) several C. glutamicum and Brevibacterium flavum strains as preferred L-threonine producing strains (column 2, lines 45-54), (2) the C. glutamicum hom gene as taught by Peoples et al. as a preferred hom gene (column 4, lines 65-67), (3) the C. glutamicum pyc gene as taught by Peters-Wendisch et al. as a preferred pyc gene (column 5, lines 8-10), (4) the C. glutamicum thrE gene as contained in the biological deposit DSM 12840 (column 5, lines 16-17) as a preferred thrE gene, and (5) the C. glutamicum mqo gene as taught by Moleenar et al. as a preferred mqo gene (column 5, lines 11-13). Also, overexpression of genes by increasing their copy number or by operatively linking genes to promoters is well known and widely practiced in the art. Therefore, claims 19-21, 23-25, 35, 40-42, 44-46, 56 of the instant application are deemed obvious over claim 6 of U.S. Patent No. 6596516 since the process of claims 19-21, 23-25, 35, 40-42, 44-46, 56 is an obvious variation of preferred embodiments in the patent.

In regard to claims 26-28, 30-34, 36-37, 47-49, 51-55, 57-58 of the instant application, these claims are directed in part to a process requiring the fermentation of L-threonine producing C. glutamicum or Brevibacterium lactum wherein the C. glutamicum or B. lactum has been transformed with the pZ1thrE plasmid contained in biological deposit DSM12840, wherein said plasmid contains a polynucleotide encoding a threonine export carrier protein, wherein said threonine export carrier protein comprises SEQ ID NO: 2, wherein said polynucleotide is overexpressed by increasing its copy number or by operatively linking it to a promoter, and wherein in addition to the polynucleotide encoding the

threonine export carrier protein, the C. glutamicum pyc gene, the C. glutamicum mqo gene, and/or the C. glutamicum hom gene are also overexpressed by increasing their copy number or by operatively linking said genes to a promoter. The scope of claim 6 in U.S. Patent No. 6596516 has been described above. As indicated above, the specification in U.S. Patent No. 6596516 discloses biological deposit DSM12840 as containing a polynucleotide encoding a C. glutamicum threonine export carrier protein. The specification in the instant application discloses in Example 3 that the coding portion of the thrE gene from C. glutamicum ATCC 13032 was cloned in a pZ1 plasmid and the resulting plasmid, pZ1thrE, was deposited in a B. flavum strain deposited as DSM12840 (paragraph 63). Also, as indicated above, the threonine export carrier protein of C. glutamicum ATCC 13032 has the same amino acid sequence as that of C. glutamicum ATCC 14752, therefore the threonine export carrier protein encoded in plasmid pZ1thrE comprises SEQ ID NO: 2. As such, claims 26-28, 30-34, 36-37, 47-49, 51-55, 57-58 are also deemed obvious over claim 6 of U.S. Patent No. 6596516 since the process of claims 26-28, 30-34, 36-37, 47-49, 51-55, 57-58 of the instant application is an obvious variation of preferred embodiments in the patent.

20. This rejection was previously applied to now canceled claims 6-8, 10-14, 16-18. Applicants argue that this rejection should not be extended to new claims 19-34 because nowhere in the specification of the instant application or in the new claims there is a discussion or teaching in regard to combining the attenuated glyA gene with one or more overexpressed genes selected from the group consisting of C. glutamicum pyc gene, C. glutamicum mqo gene, C. glutamicum hom gene, and the C. glutamicum hom^{dr} allele. Applicants submit that the invention in the instant application is directed to a fermentative process in Corynebacterium or Brevibacterium wherein the C. glutamicum thrE gene is overexpressed and may be combined with the overexpression of one of the following C. glutamicum genes: pyc, hom, hom^{dr}, and mqo.

21. Applicant's arguments have been fully considered but are not deemed persuasive to avoid the rejection of new claims 19-21, 23-28, 30-37, 40-42, 44-49, 51-58. Detailed reasons as to why this

rejection is proper are presented above. In regard to Applicant's arguments indicating that combination of the attenuated glyA gene with the overexpressed C. glutamicum genes recited in the claims is not taught or suggest in the instant application are not relevant to the instant discussion in view of the fact that claim 6 of U.S. Patent No. 6596516 is considered to be directed to a species of what is being claimed in the instant application, which renders the claimed invention obvious. It is noted that claim 6 is more limited as it also requires the attenuation of the glyA gene. In contrast, the claims in the instant application are deemed generic, as they do not exclude the attenuation of other genes or even the overexpression of additional genes not recited in the claims. The claims in the instant application do not exclude the attenuation of the glyA gene. Furthermore, as indicated above, claim 6 requires the attenuation of the glyA gene and the overexpression of one or more of the genes recited. As such, one of the combinations encompassed by claim 6 is the overexpression of the thrE gene, pyc gene, mqo gene, and hom gene, as well as the attenuation of the glyA gene. This combination would render the claimed invention obvious for the reasons discussed above.

Allowable Subject Matter

22. Claims 29, 38, 50, 59 appear to be allowable over the prior art of record but are objected to since they depend upon base rejected claims.

Conclusion

23. No claim is in condition for allowance.

24. Applicant's addition of new claims 19-60 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

25. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

26. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
August 18, 2004

REBECCA E. PRUTY
PRIMARY EXAMINER
~~1600~~
1600